

We claim:

1. A system for diagnosing a non-central nervous system (non-CNS) disorder in a subject comprising:

5 a sampling device to obtain a central nervous system (CNS) sample;
a gene expression detection device that generates gene expression data for one or more genes in the CNS sample;
a reference gene expression profile for a specific non-CNS disorder; and
a comparator that receives and compares the gene expression data with the
10 reference gene expression profile.

2. A system for diagnosing a non-central nervous system (non-CNS) disorder in a subject comprising

15 an imaging device to obtain an image of gene expression of one or more genes in the central nervous system (CNS) and generate gene expression data for the one or more genes;
a reference gene expression profile for a specific non-CNS disorders; and
a comparator that receives and compares the gene expression data with the reference gene expression profile.

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3. A method of diagnosing a non-central nervous system (non-CNS) disorder in a subject, the method comprising:

detecting expression of one or more genes in a CNS sample of the subject;
generating gene expression data from the detected expression;
25 obtaining a reference gene expression profile for a specific non-CNS disorders;
and

comparing the gene expression data with the reference gene expression profile, wherein a match of the CNS sample gene expression data to the reference gene expression profile indicates the subject has or will develop the non-CNS disorder.

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4. The system of claim 1 or 2 or the method of claim 3, wherein the CNS sample is a cerebrospinal fluid (CSF) sample, and the gene expression data corresponds to a protein in the CSF.
- 5 5. The system of claim 1 or 2 or the method of claim 3, wherein the CNS sample is a bodily fluid sample that comprises a protein expressed by a gene in the CNS, and the gene expression data corresponds to the presence or level of the protein in the sample.
6. The system of claim 1 or 2 or the method of claim 3, wherein the CNS sample is a
10 bodily fluid sample that comprises a protein whose presence or level in the sample is affected by a gene expressed in the CNS, and the gene expression data corresponds to the presence or level of the protein in the sample.
7. The system or method of claim 5 or 6, wherein the protein is selected from the
15 group consisting of a hormone, a growth factor, an immune system component, and a cytokine.
8. The system or method of claim 5 or 6, wherein the protein is encoded by any of the genes listed in any of FIGS. 1, 50, and 54, or a human or other mammalian homolog
20 thereof.
9. The system or method of claim 5 or 6, wherein the gene encodes a gene product selected from the group consisting of hepatocyte growth factor (HGF), apherin A3, chemokine (C-C motif) ligand 4, growth differentiation factor-9b (GDF-9b); bone
25 morphogenetic protein 15 (BMP 15), neuroblastoma suppressor of tumorigenicity 1, melanocyte proliferating gene 1, and fibroblast growth factor 22 (FGF 22).
10. The system of claim 1 or 2 or the method of claim 3, wherein the CNS sample is a sample of one or more cells from the brain, and the gene expression data corresponds to
30 an nucleic acid molecule or protein in the sample.

11. The system or method of claim 10, wherein the brain cells are selected from the group consisting of cells from: the hypothalamus, the midbrain, the prefrontal cortex and the striatum.

5 12 The system or method of claim 10, wherein the nucleic acid molecule comprises mRNA corresponding to the gene.

13. The system of claim 1 or 2 or the method of claim 3, wherein two or more reference gene expression profiles are used, each specific for a different non-CNS
10 disorder.

14. The system of claim 1 or 2 or the method of claim 3, wherein the non-CNS disorder is selected from the group consisting of cancer, rheumatoid arthritis, asthma, diabetes, and obesity.

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15. The system of claim 1 or 2 or the method of claim 3, wherein the non-CNS disorder is a carcinoma.

16. The system of claim 1 or 2 or the method of claim 3, wherein the non-CNS
20 disorder is a solid tumor less than 0.5 cm in diameter.

17. The system of claims 1 or 2, or the method of claim 3, wherein the gene expression data comprises data for a plurality of genes in the CNS sample, and comprises a gene expression profile.

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18. The method of claim 3, further comprising
obtaining a control gene expression profile corresponding to one or more healthy subjects; and

comparing the gene expression data with the control gene expression profile,
30 wherein a match of the CNS sample gene expression data to the control gene expression profile indicates the subject does not have and will not develop the non-CNS disorder.

19. The system of claim 1 or 2, or the method of claim 3, wherein the gene expression is detected using a microarray assay.

20. The system of claim 1 or 2, or the method of claim 3, wherein the subject is a human.

21. A method of diagnosing a non-central nervous system (non-CNS) disorder in a subject, the method comprising:

obtaining a test gene expression profile for two or more central nervous system (CNS) genes from the subject;

obtaining a reference gene expression profile for a specific non-CNS disorder; and

comparing the test gene expression profile with a reference gene expression profile, wherein a test gene expression profile that matches the reference gene expression profile indicates the subject has or will develop the non-CNS disorder.

22. The method of claim 21, further comprising generating a record of the result of the comparing step; and optionally transmitting the record to the subject, health care provider, or other party.

23. The method of claim 21, wherein the non-CNS disorder is selected from the group consisting of: cancer, rheumatoid arthritis, asthma, diabetes and obesity.

24. The method of claim 21, wherein obtaining the test gene expression profile comprises detecting mRNA corresponding to the two or more CNS genes.

25. The method of claim 21, wherein obtaining the test gene expression profile comprises detecting polypeptide products encoded by the two or more CNS genes.

26. The method of claim 21, wherein test gene expression profiles are obtained for a plurality of CNS genes.

27. The method of claim 21, wherein obtaining the test gene expression profile comprises performing a microarray assay.

28. A computer-readable medium comprising a data set corresponding to a reference gene expression profile comprising expression data of 5 or more genes, wherein each of the 5 or more genes is differentially expressed in a central nervous system (CNS) sample of a mammal having a specific non-CNS disorder compared to the same 5 or more genes in a mammal not having the specific non-CNS disorder; wherein the data set is used to diagnose a non-CNS disorder.

29. The computer-readable medium of claim 28, wherein the reference gene expression profile comprises expression data of 5 or more genes selected from any of the genes listed in one or more of FIGs. 29-1 to 29-6; 32-1 to 32-6; or 35-1 to 35-6 for breast cancer; FIGs. 30-1 to 30-6; 33-1 to 33-6; or 36-1 to 36-6 for colon cancer; FIGs. 31-1 to 31-6; 34-1 to 34-6; or 37-1 to 37-6 for lung cancer; FIG. 50 for arthritis; or FIG. 54 for asthma.

30. The computer-readable medium of claim 28, wherein the 5 or more genes are selected from any one of the following groups of genes:

Breast Cancer: Nedd8 (FIG. 29-1), Col4a3bp (FIG. 29-2), Bgn (FIG. 29-4), Sox5 (FIG. 29-5), Slc38a4 (FIG. 32-1), Tom1 (FIG. 32-2), Calr (FIG. 32-4), Itgae (FIG. 32-5), Ttrap (FIG. 35-1), Pex11b (FIG. 35-2), Sema7a (FIG. 35-4), and Stam2 (FIG. 35-5);

Colon Cancer: Nmb (FIG. 30-1), Ryr2 (FIG. 30-2), Trfr (FIG. 30-4), Mfap5 (FIG. 30-5), Prrg2 (FIG. 33-1), Faim (FIG. 33-2), Mgrn1 (FIG. 33-4), Stch (FIG. 33-5), Lhb (FIG. 36-1), Prm3 (FIG. 36-2), Crry (FIG. 36-4), and Timp4 (FIG. 36-5);

Lung cancer: Nmb (FIG. 31-1), Pcdh8 (FIG. 31-2), Rock2 (FIG. 31-4), Angptl3 (FIG. 31-5), Sqstm1 (FIG. 34-1), Kcnip2 (FIG. 34-2), Oxt (FIG. 34-4), Myh4 (FIG. 34-5), Enc1 (FIG. 37-1), Gsg1 (FIG. 37-2), Srr (FIG. 37-4), and Ndph (FIG. 37-5);

Arthritis: Bcl2l (FIG. 51A), P2rx1 (FIG. 51B), Pafah1b1 (FIG. 51B), Kcna3 (FIG. 51C), Taf1b (FIG. 51C), Slc38a3 (FIG. 51D), Hprrt (FIG. 52A), C1d (FIG. 52B), Car11 (FIG. 52D), Dusp3 (FIG. 52D), Gabrr2 (FIG. 53C), and Aatk (FIG. 53D); and

Asthma: Rasa3 (FIG. 55B), Tnk2 (FIG. 55B), H28 (FIG. 55C), Diap2 (FIG. 55C), Lgals6 (FIG. 56A), Reck (FIG. 56A), Whrn (FIG. 56A), Stk22s1 (FIG. 56B), CD47 (FIG. 57A), Jund1 (FIG. 57A), Cstb (FIG. 57B), and Desrt (FIG. 57B).

- 5 31. A method of identifying a disease surveillance gene for a non-central nervous system (non-CNS) disorder in a human, the method comprising:
- inducing a non-CNS disorder in a test experimental animal;
- comparing expression of a gene in a CNS sample from the test experimental animal to expression of the gene in a CNS sample from a control experimental animal;
- 10 and
- selecting as a disease surveillance gene a human homolog of a gene that is differentially expressed in the CNS sample from the test experimental animal compared to the CNS sample from the control experimental animal.
- 15 32. The method of claim 31, wherein a non-CNS neoplasm is induced by chemical or radiation mutagenesis.
33. The method of claim 31, wherein a non-CNS neoplasm is induced by administering a neoplastic cell to the experimental animal.
- 20 34. The method of claim 31, wherein the experimental animal is an animal model of rheumatoid arthritis, diabetes, asthma, obesity, or diabetes.
35. The method of claim 31, wherein the experimental animal is a mouse or non-
- 25 human primate.
36. The system or method of any of the preceding claims, wherein the subject lacks a clinical sign of a disorder as evaluated by imaging analysis.
- 30 37. The system or method of any of the preceding claims, wherein the subject has a family history of the disorder.

38. The system or method of any of the preceding claims, wherein the subject is a carrier of a gene associated with an increased risk of developing the disorder.

5 39. The method of claim 38, wherein the subject is a carrier of the BRCA1, BRCA2, hMSH2, hMLH1, or hMSH6 gene.

40. A method of generating a reference gene expression profile of one or more genes that are differentially expressed in a CNS sample of a mammal having a specific non-
10 CNS disorder, the method comprising:
 obtaining a control mammal not having the specific non-CNS disorder;
 obtaining a diseased mammal of the same type as the control mammal that has the specific non-CNS disorder;
 obtaining a first CNS sample from the control mammal and a second CNS sample
15 from the diseased mammal;
 generating a first gene expression profile from the first CNS sample and a second genetic expression profile from the second CNS sample;
 comparing the first and second genetic expression profiles;
 selecting a set of genes from the second genetic expression profile that are
20 differentially expressed; and
 preparing the reference gene expression profile from expression data from the selected genes.

41. A reference gene expression profile corresponding to the presence of a non-
25 central nervous system (non-CNS) disorder in a mammal, comprising expression data of 5 or more genes, wherein each of the 5 or more genes is differentially expressed in a central nervous system (CNS) sample of a mammal having a specific non-CNS disorder compared to the same 5 or more genes in a mammal not having the specific non-CNS disorder.

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42. The reference gene expression profile of claim 41, wherein the reference gene expression profile comprises expression data of 5 or more genes selected from any genes listed in one or more of FIGs. 29-1 to 29-6; 32-1 to 32-6; or 35-1 to 35-6 for breast cancer; FIGs. 30-1 to 30-6; 33-1 to 33-6; or 36-1 to 36-6 for colon cancer; FIGs. 31-1 to 31-6; 34-1 to 34-6; or 37-1 to 37-6 for lung cancer; FIG. 50 for arthritis; or FIG. 54 for asthma.

43. The reference gene expression profile of claim 41, wherein the 5 or more genes are selected from any one of the following groups of genes:

10 Breast Cancer: Nedd8 (FIG. 29-1), Col4a3bp (FIG. 29-2), Bgn (FIG. 29-4), Sox5 (FIG. 29-5), Slc38a4 (FIG. 32-1), Tom1 (FIG. 32-2), Calr (FIG. 32-4), Itgae (FIG. 32-5), Ttrap (FIG. 35-1), Pex11b (FIG. 35-2), Sema7a (FIG. 35-4), and Stam2 (FIG. 35-5);

Colon Cancer: Nmb (FIG. 30-1), Ryr2 (FIG. 30-2), Trfr (FIG. 30-4), Mfap5 (FIG. 30-5), Prrg2 (FIG. 33-1), Faim (FIG. 33-2), Mgrn1 (FIG. 33-4), Stch (FIG. 33-5), 15 Lhb (FIG. 36-1), Prm3 (FIG. 36-2), Crry (FIG. 36-4), and Timp4 (FIG. 36-5);

Lung cancer: Nmb (FIG. 31-1), Pcdh8 (FIG. 31-2), Rock2 (FIG. 31-4), Angptl3 (FIG. 31-5), Sqstm1 (FIG. 34-1), Kcnp2 (FIG. 34-2), Oxt (FIG. 34-4), Myh4 (FIG. 34-5), Enc1 (FIG. 37-1), Gsg1 (FIG. 37-2), Srr (FIG. 37-4), and Ndph (FIG. 37-5);

Arthritis: Bcl2l1 (FIG. 51A), P2rx1 (FIG. 51B), Pafah1b1 (FIG. 51B), Kcna3 20 (FIG. 51C), Taf1b (FIG. 51C), Slc38a3 (FIG. 51D), Hprrt (FIG. 52A), C1d (FIG. 52B), Car11 (FIG. 52D), Dusp3 (FIG. 52D), Gabrr2 (FIG. 53C), and Aatk (FIG. 53D); and

Asthma: Rasa3 (FIG. 55B), Tnk2 (FIG. 55B), H28 (FIG. 55C), Diap2 (FIG. 55C), Lgals6 (FIG. 56A), Reck (FIG. 56A), Whrn (FIG. 56A), Stk22s1 (FIG. 56B), CD47 (FIG. 57A), Jund1 (FIG. 57A), Cstb (FIG. 57B), and Desrt (FIG. 57B).

25 44. A method of treating a subject, the method comprising:
diagnosing a non-central nervous system (non-CNS) disorder according to the method of claim 3 or 21; and
administering to the subject a therapeutic agent for the disorder.

30 45. The method of claim 44, wherein the therapeutic agent is chemotherapeutic agent.

46. The method of claim 45, wherein the chemotherapeutic agent is selected from the group consisting of: an antitubulin/antimicrotubule drug, a topoisomerase I inhibitor, an antimetabolite, and an alkylating agent.

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